GIVING FULL MEASURE TO COUNTERMEASURES: ADDRESSING PROBLEMS IN THE DoD PROGRAM TO DEVELOP MEDICAL COUNTERMEASURES AGAINST BIOLOGICAL WARFARE AGENTS

Statement of

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Good afternoon, Mr. Chairman and members of the Committee. My name is Ronald Saldarini. I am currently a scientific and business consultant to the vaccine and pharmaceutical industry. From 1986 to 1999, I was president of the global vaccine business of American Cyanamid (Lederle Praxis) and American Home Products (Wyeth Lederle). I am here today as a member of the Committee on Accelerating the Research, Development, and Acquisition of Medical Countermeasures Against Biological Warfare Agents of the Institute of Medicine (IOM) and the National Research Council (NRC). The Institute of Medicine and National Research Council are part of the National Academies, chartered by Congress in 1863 to advise the government on matters of science and technology.

The report from which I provide my testimony was the product of a study initiated in 2002 in response to a congressional mandate in the National Defense Authorization Act for Fiscal Year 2002 (P.L. 107-107). Seeking to speed the availability of new medical countermeasures (vaccines, therapeutic drugs, and antitoxins) against biological warfare agents, Congress called for a study to identify new approaches to accelerate the review and approval process for these products and to identify methods for ensuring that new countermeasures will be safe and effective. The specific charge to the study committee called for examining the acquisition process of the Department of Defense (DoD) for drugs and vaccines intended to serve as biowarfare countermeasures. The scope of the committee's assessment included early science and technology development (research and development program elements 6.1, 6.2, 6.3) and advanced development (program elements 6.4, 6.5) through approval and licensure of products by the Food and Drug Administration (FDA). The committee's report *Giving Full Measure to Countermeasures: Addressing Problems in the*

DoD Program to Develop Medical Countermeasures Against Biological Warfare Agents was released in January 2004.

I want to emphasize that the study did not examine production and procurement processes for medical countermeasures. Furthermore, the committee was not asked to assess the nature or extent of any biological warfare threat or to compare the value to DoD of developing medical countermeasures against biological warfare agents relative to the pursuit of other obligations. The committee viewed its task as resting on the premise that biological weapons pose a threat to the health of military personnel, and therefore additional FDA-licensed medical countermeasures are urgently needed.

THE CONTEXT FOR DEVELOPMENT OF MEDICAL COUNTERMEASURES

Developing new vaccines and drugs is challenging, both financially and technically. Estimates of the average cost of bringing a new drug to market have ranged from $110 million to $802 million. As few as one candidate product in 5,000 may reach clinical testing, and only 20 percent of candidates that begin clinical testing reach licensure. Such estimates are based primarily on data for new drugs, with few equivalent estimates available for vaccines and other biologics.

The drug and vaccine development process is also time consuming. One industry estimate presented to the committee was 7 to 12 years for vaccine development, but experience has shown that successful completion of clinical testing alone can take as long as 20 years.

Although new techniques are likely to speed the discovery of some candidate countermeasures, they are unlikely to accelerate some of the most time-consuming parts of the product development process, including the crucial assessments of a product's safety and

efficacy. Biodefense products pose special scientific, regulatory, and ethical challenges because it is generally unacceptable to expose humans to biowarfare agents to establish the efficacy of medical countermeasures.

Until the late 1990s, federally funded efforts to develop medical biodefense countermeasures were based primarily in DoD. Since the late 1990s, a substantial research effort has emerged within the Department of Health and Human Services, and "Project BioShield" now aims to create financial incentives for the pharmaceutical industry to manufacture and license medical countermeasures. The upsurge in funding and effort aimed at protecting the civilian population against bioterrorism will undoubtedly result in new technologies and products that can also help protect military personnel against biological warfare. Nevertheless, the committee saw a need for a continued DoD program because of a concern that reliance on a program to protect the civilian population may not meet unique military needs for battlefield protection.

COMMITTEE CONCLUSIONS CONCERNING DOD EFFORTS TO DEVELOP MEDICAL COUNTERMEASURES

On the basis of its review, conducted in 2003, the committee concluded that the biodefense efforts of DoD were poorly organized to develop and license vaccines, therapeutic drugs, and antitoxins to protect members of the armed forces against biological warfare agents.

The committee found that DoD's work on medical biodefense countermeasures was part of a program that addresses medical and nonmedical countermeasures against both chemical and biological warfare threats. Responsibility for centralized oversight of the Chemical and Biological Defense Program was assigned to the Assistant to the Secretary of Defense for

Nuclear and Chemical and Biological Defense Programs. However, the operational reality was a fragmented process that put research planning and activities for medical countermeasures under the direction of the Defense Threat Reduction Agency in the Office of the Secretary of Defense, while the execution of those activities (i.e., basic and applied research in a laboratory setting) rested largely with personnel of the U.S. Army Medical Research and Materiel Command, which reports to the Army Surgeon General. Management of the acquisition process for candidate countermeasures that have reached the stage of advanced development was the responsibility of the Joint Program Executive Office for Chemical and Biological Defense, which operates under the direction of Army acquisition officials. The scientific and technical work of product development was being carried out by a variety of private sector firms and integrated through the prime systems contract with DynPort Vaccine Company. Program planning and budgeting were directed from within yet another DoD organization, the Joint Chiefs of Staff.

In addition to the fragmentation of responsibility and authority, the committee found changing strategies that resulted in lost time and expertise and a lack of financial commitment commensurate with the requirements of program goals.

This serious situation existed despite declarations that biological warfare poses a significant threat to the safety and effectiveness of the nation's armed forces, the vaccination of large numbers of military personnel against anthrax and smallpox, a DoD commitment to acquire vaccines against all validated biological warfare threats, and concerns about new bioengineered microbial threats.

The committee concluded that DoD had not given the technically difficult, expensive, and time-consuming task of development and licensure of new biodefense vaccines and

therapeutic products sufficient priority to produce the intended results. The disjointed and ineffective management and inadequate funding of DoD's efforts were viewed as clear indications that DoD leaders lacked an adequate grasp of the commitment, time, scientific expertise, organizational structure, and financial resources required for success in developing vaccines and other pharmaceutical products. The committee emphasized that the fragmented half-measures of DoD's effort could not be expected to succeed.

RECOMMENDATIONS FOR ACTION

Improving and accelerating DoD's efforts to develop and license new biodefense vaccines and therapeutic products to protect against present and future biological warfare threats will require strong and creative scientific leadership and a sustained commitment of adequate funding and other resources. Maintaining the status quo in DoD only assures a long, costly, and perhaps fruitless wait for new vaccines and therapeutic products, in the committee's view.

The IOM/NRC committee recommended action in several areas to help make the DoD work on medical countermeasures more effective:

- **Make the Development of Medical Countermeasures a Priority**

To ensure that DoD has an effective research and development program for medical biodefense countermeasures, the committee made the following recommendation: The Secretary of Defense and Congress must make the DoD program for medical biodefense countermeasures a high priority.

If the development of medical countermeasures becomes a priority, the committee identified other changes that would have to follow to establish a sound infrastructure for

integrated and comprehensive management of all aspects of the research and development work:

- organizing the program to promote accountability and effective coordination throughout all phases of research, development, and product approval;
- installing scientifically knowledgeable leaders with expertise in the development of vaccines and pharmaceutical products;
- supporting the development of a strong scientific infrastructure; and
- providing the necessary funding to achieve program goals.

- **Create a Medical Biodefense Agency in DoD**

The committee specifically recommended that Congress should *authorize the creation of the Medical Biodefense Agency*, a new DoD agency responsible for the research and development program for medical countermeasures against biological warfare agents.

As proposed by the committee, this agency would *report directly to the Under Secretary of Defense for Acquisition, Technology, and Logistics*.

The Medical Biodefense Agency should c*onsolidate the functions and resources of several existing activities*. The competing lines of authority and multiple reporting relationships that the committee found in the DoD system are not adequate. The functions of existing medical biodefense programs, along with their personnel and funding, should be transferred to the new Medical Biodefense Agency. This would include the medical biodefense component of the Chemical and Biological Defense Program, including units within the Army such as the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and related activities in the Defense Advanced Research Projects Agency

(DARPA), as well as the medical biodefense component of the Chemical Biological Medical Systems in the Joint Program Executive Office for Chemical and Biological Defense.

In addition, *the research and development program for medical countermeasures against infectious diseases should also be transferred into the Medical Biodefense Agency*. DoD's programs to develop medical countermeasures against biological warfare agents and against infectious diseases of military significance address similar scientific and technological questions and require closely related expertise and facilities. Also, with concerns about biological warfare threats expanding to include a wider range of naturally occurring and novel biological agents, the line between the two programs is becoming even less distinct and meaningful than it was in the past.

The agency should have *a highly qualified director with strong experience in vaccine and drug research and development and manufacturing, including the rapidly evolving contributions of biotechnology*. It is essential that the agency head have *direct authority over the agency's budgeting and over its full range of management and operational activities*, which should extend from basic research through full-scale production. An organizational approach that creates competing lines of authority and multiple reporting relationships, as the matrix scheme observed by the committee does, is not adequate to address the multiple management and scientific challenges that DoD faces.

Of particular importance is ensuring that the Medical Biodefense Agency has the *authority to manage the transition of candidate products from the science and technology stage into, and their progress through, the DoD acquisition system*. The Medical Biodefense Agency should have the authority to use funds from science and technology accounts (e.g.,

budget activity 6.3) to support Phase 1 and even Phase 2 clinical trials before a candidate product is subject to acquisition system review.

As proposed by the committee, the Medical Biodefense Agency would rely on *both its intramural research and development program and also build a strong extramural program* to bring the expertise and creativity of industry and the academic community to the task. The agency should focus on meeting unique DoD needs, while ensuring that DoD's program is coordinated with and takes full advantage of related NIH activities.

Based on the scope of DoD's medical biodefense program and the experience of other relevant government agencies and the private sector, *the committee found the DoD program to be underfunded*. Nevertheless, the committee advised that the program should be better focused before any substantial increase in funding occurs. A need for increased funding should be expected if the program successfully expands its extramural research, thus needing to absorb personnel and facility costs currently covered separately in accounts of the military services. Further increases in funding are also likely as products move into later phases of development, which traditionally are more costly. Supplemental funding is also needed for renovation or replacement of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) facility, with its unique animal research resources and specialized laboratory facilities.

The committee was strongly persuaded that creation of the Medical Biodefense Agency would be the most effective means of improving DoD's research and development program for medical biodefense countermeasures. This approach allows for continued DoD control over program priorities, integrated planning and management of all stages in the development of medical biodefense countermeasures, increased visibility of and priority for this work

within DoD, increased expertise among the program leadership and managers, enhanced opportunity for coordination with related NIH work on bioterrorism countermeasures, and expanded access to contributions from extramural researchers. At the same time, the committee acknowledged the disruption associated with establishing a new agency and the potential difficulty of attracting a director and agency staff with the necessary qualifications.

- **Establish External Oversight and Accountability for Performance**

To monitor the performance of the DoD research and development program, the committee recommended independent, external review by a standing group of experts from academia and the biotechnology and pharmaceutical industries, with that group's findings reported each year to the Secretary of Defense and the Congress.

The committee found that DoD failed to respond adequately to previous reports with similar recommendations for change. Therefore, as a last resort, if DoD does not take steps necessary to establish an effective program and make appropriate progress within 3 years (as judged by the review group), the committee recommended that all or part of this responsibility should be transferred to an agency responsible for promoting the development of medical countermeasures for bioterrorism defense.

- **Address Other Challenges Related to the Development of Medical Countermeasures**

The committee also recommended that DoD address several other issues, often in collaboration with others, to improve prospects for the successful development and licensure of medical biowarfare countermeasures. In particular, DoD will need to *establish effective collaborations with academia and industry and should reduce barriers to collaboration* posed

by complex, cumbersome contracting procedures; the potential instability of government funding; and concerns about potential liability risks.

DoD and other federal agencies will need to *meet special regulatory challenges* because efficacy studies in humans for products intended to protect against potentially lethal pathogens are generally not feasible or ethical. DoD should be part of the extensive research and testing that will be needed to establish the scientific basis for the application of new FDA regulatory guidelines that provide for using animal data for this purpose (the "Animal Efficacy Rule"). The committee also noted the need to ensure sufficient funding for FDA to sustain its added efforts to expedite the testing and review of biodefense products.

Another challenge facing DoD and others is *overcoming current and potential bottlenecks related to research resources*, including specialized laboratory facilities with appropriate biosafety features, facilities to study and house the animals that are essential for this research, and facilities that can produce small supplies of candidate countermeasures in compliance with FDA manufacturing standards.

Finally, DoD should contribute to efforts to *ensure the availability of a well-trained workforce* by defining the capabilities that scientific and technical personnel will need to conduct research and development on medical countermeasures and by aiding in the development and implementation of training programs designed to meet those needs. In addition, DoD should seek to attract and retain a skilled workforce by using available means to offer salaries that are competitive with those in academia and industry.

Thank you for the opportunity to testify. I would be pleased to answer any questions the Committee might have.